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Renal Outcomes Following Fenestrated and Branched Endografting

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WHAT THIS PAPER ADDS

This study adds new markers of renal function and renal volume, which can easily be assessed during follow up to demonstrate renal impairment. The results from this study confirm that FEVAR and BEVAR are durable options for the treatment of complex aortic aneurysms and are associated with a low renal morbidity rate, without any differences between these devices.

Objective: The purpose of this study was to analyze immediate and long-term renal outcomes (renal function and renal events) after fenestrated (FEVAR) and branched endovascular aortic aneurysm repair (BEVAR).
Methods: All FEVAR and BEVAR performed between October 2004 and October 2012 were included in this study. Post-operative acute renal failure (ARF) was defined according to the RIFLE criteria. Renal volume (calculated with a 3D workstation) and estimated glomerular filtration rate (GFR) (estimated with the Modification of Diet in Renal Disease [MDRD] formula) were evaluated before the procedure, before discharge, 12 months after, and yearly thereafter. Renal stent occlusion, dissection, fracture, stenosis, kink, renal stent related endoleak, and renal stent secondary intervention were all considered "renal composite events" and analyzed. A time to event analysis was performed for renal events and secondary renal interventions.
Results: 225 patients were treated with FEVAR and BEVAR. Renal target vessels ($n = 427$) were perfused by fenestrations ($n = 374$), or branches ($n = 53$). Median follow up was 3.1 years (2.9–3.3 years). Technical success was achieved in 95.5% of patients. Post-operative ARF was seen in 64 patients (29%). Mean total renal volume and eGFR at 1 year, 2 year, and 3 year follow up were significantly lower when compared with pre-operative levels (after BEVAR and FEVAR); the decrease at 3 years was 14.8% (6.7%; 22.2%) ($p = .0006$) for total renal volume and 14.3% (3.1%; 24.3%) ($p = .02$) for eGFR. The 30 day and 5 year freedom from renal composite event was 98.6% (95.8–99.6%) and 84.5% (76.5–89.9%) after FEVAR and BEVAR (NS). The 30 day and 5 year freedom from renal occlusion was 99.5% (96.7–99.9%) and 94.4% (89.3–97.1%) after FEVAR and BEVAR (NS).
Conclusion: FEVAR and BEVAR are durable options for the treatment of complex aortic aneurysms and are associated with low renal morbidity, without differences between devices types. The clinical impact of decreasing renal volume over time in these patients is yet to be fully understood.

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INTRODUCTION

The first reports of endovascular treatment of complex juxtarenal/pararenal aortic aneurysms (JR-PRAA) and thoraco-abdominal aortic aneurysms (TAAA) were published by Faruqui et al. in 1999[1] and Chuter et al. in 2001.[2] Since that time, the technology has come into mainstream clinical use, and a recent review comparing endovascular and open repair[3] of complex aneurysms reported a 2.4% 30 day mortality rate after fenestrated endovascular repair (FEVAR) versus 3.4% after open repair and 5.3% following chimney repair.

Post-operative renal impairment is one of the most frequent major complications associated with complex aneurysm treatment using any modality. Nordon et al.[4] described in their systematic review an incidence of early transient renal failure of 15% following FEVAR compared with 20% after open repair. Mid- and long-term renal outcomes after complex endovascular repair are associated with "branch instability" as defined by Mastracci et al[5]: branch occlusion, device migration affecting a branch, branch related growth, or the need for any secondary

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intervention. However, because several definitions of renal impairment are used in the literature describing outcomes for fenestrated repair, it is difficult to perform an effective comparison across all reports. The purpose of this study was to analyze immediate and long-term renal outcomes after complex endovascular repair performed in a high volume center.

MATERIAL AND METHODS

Study population

All complex endovascular repairs (including both FEVAR [fenestrated endovascular aortic aneurysm repair] and BEVAR [branched endovascular repair]) performed in a single institution between October 2004 and October 2012 were included in this study. Ruptured aneurysms and acute aortic dissections were excluded.

All patients were treated by the same group of vascular surgeons at a single high volume academic center. In order to have a follow up $\geq$ 12 months, patients treated after October 2012 were not included. All endovascular procedures were performed with fenestrated or branched endografts manufactured by Cook Medical (Bloomington, IN, USA). The FEVAR and BEVAR procedures were performed with a mobile C-arm. In accordance with the literature,[6,7] iso-osmolar iodixanol contrast media (Visipaque, 320 mg I/mL, GE Healthcare, Dublin, Ireland) was used when the estimated glomerular filtration rate (eGFR) was $<$ 60 mL/min/1.73 m^2, and low osmolar iohexol contrast media (Omnipaque, 300 mg I/mL, GE Healthcare) in the remaining patients.

Patient data were prospectively collected in an electronic database and electronic or paper medical records were also reviewed retrospectively for the purpose of this study. Baseline demographics and risk factors, including medications with renal impact and intra-operative contrast volume, were collected.

Renal function

eGFR was determined using the abbreviated MDRD study equation (eGFR mL/min/1.73 m^2 = 186 $\times$ [serum creatinine]$^{-1.154}$ $\times$ [age]$^{-0.203}$ $\times$ [0.704 if female] $\times$ [1.210 if African American]).[8] The eGFR was calculated and collected pre-operatively, on the first post-operative day, on the day of discharge, and yearly thereafter. Chronic kidney disease (CKD) was defined as eGFR $<$ 60 mL/min/1.73 m^2 based on the National Kidney Foundation/Kidney Disease Outcome Quality Initiative (NKF/KDOQI).[8] The RIFLE classification,[9] based on eGFR evaluated 48–72 hours after the procedure, was used for the post-operative diagnosis of acute renal failure (ARF), defined as an increase in eGFR of at least 25%.

Imaging analysis

Pre-operative multi-detector computed tomography (MDCT) scans were obtained in all patients. A CT scan was also performed at discharge, 12 months, and yearly thereafter. All CT scans analyzed in this study were performed during the standard follow up protocol after FEVAR/BEVAR. Renal duplex imaging was also performed to supplement data.

MDCT scans were loaded into a workstation (AquariusNET software, TeraRecon Inc., San Mateo, CA, USA) for imaging analysis by one of the authors (T.M.G.). A standardized protocol for assessment was developed. The longest cranio-caudal renal length was selected from the three dimensional volume rendered reconstruction and measured on both sides. Combined kidney length measurements (mean renal length) were calculated for each pair of kidneys. The volume of each kidney was calculated by the following method: a semi-automated post-processing treatment extracted the renal contour. The pelvicalyceal systems, fat and vessels in the renal sinus, and renal cysts were excluded by manual correction on multiplanar views in case they had been automatically included. Then, the renal volume was automatically measured (in cm^3). Combined kidney volumes (sum of right and left volumes) were also calculated for each pair of kidneys. Intra- and inter-observer differences were analyzed using the intraclass correlation coefficient (ICC). Ten patients included in a previous study with similar analysis were analyzed three times by two physicians. No significant intra- or inter-observer variation were observed (volume: ICC = 0.999 [CI 95%, 0.998–1.000] [$p < .000$]; length: ICC = 0.991 [CI 95%, 0.980–0.996] [$p < .000$]).

The renal artery angles were measured by the method described by Conway et al.[10]: a semi-automated centerline was generated from the aortic bifurcation to the level of the diaphragm. The centerline was assessed with multiplanar reconstruction views perpendicular to the centerline of flow. A positive renal artery implantation angle (RAIA) was defined as an angle above the horizontal plane perpendicular to the aortic centerline of flow at the mid level of the renal ostia. A quantitative angular measurement for the RAIA was taken using the angular measurement tool provided in the AquariusNET software. The process was repeated for each renal artery, stented or involved in the graft including accessory renal arteries, pre-operatively and at each follow up. Accessory renal arteries were measured and recorded only if they were included in the device.

Renal outcome events were assessed using the MDCT scan and were complemented with duplex ultrasound. Duplex ultrasound criteria applied were defined by Mohabbat et al.[11] and MDCT scan interpretation was based on the methods described by Dowdall et al.[12] Imaging outcomes were defined according to reporting standards[13] and to modifications assessed by Mastracci et al.[5] Renal composite outcome included branch occlusion, in-stent stenosis, stent kinking, stent fracture, and renal related endoleak.

Statistical analysis

Analyses were conducted using SAS software (SAS version 9.2, SAS Institute Inc., Cary, NC, USA).

Continuous variables are expressed as mean ± SD or median (25th–75th percentile), as appropriate. Categorical variables are presented as absolute numbers and percentages. The comparison of subjects with a fenestrated device to subjects with a multi-branched device was performed using the Student *t* or Mann–Whitney U tests according to normality assessed by the Shapiro–Wilk test and using the chi-square test or the Fisher exact test, as appropriate, for proportions of categorical variables.

Longitudinal data (serum creatinine, eGFR, renal volumes and lengths) were analyzed using repeated measures analysis of covariance (PROC MIXED) with time as a categorical covariate (pre-operatively, at 1 year, 2 years, and 3 years of follow up), and with a REPEATED statement for within patient correlation. Data were log-transformed because of skewed distributions. The repeated measures covariance structure was selected with likelihood ratio tests in case of nested models or using the Bayesian Information Criterion for non-nested models. Multivariate models were built by first including all predictors and then using a backward selection to reduce the model. In case of a significant interaction between two predictors, the two main effect terms remained in the model, even if not significant. Regression underlying assumptions were visually inspected with residual plots. Influential observations were assessed using Cook's distance and leverage measure and removed from the models to ensure that conclusions remained valid. Parameters of the models were tested with polynomial contrasts, and means and 95% confidence intervals were estimated using least square means.

Event free survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Median follow up time was estimated with the reverse Kaplan–Meier method. Univariate Cox analyses were performed to identify independent predictors of event (renal event – being censored at the time of death, death). The log-linearity assumption for continuous variables and the proportional hazard assumption were tested by Kolmogorov-type supremum tests as implemented in the PROC PHREG and visually inspected with residual plots. In case of violation of the former assumption, the continuous variable was dichotomized, the cut off value being visually established and maximizing the Harrell c statistics (as a measure of calibration) and the Kent and O'Quigley ρ^2 (as a measure of discrimination); in case of violation of the latter assumption, a piecewise model was used to model the hazard ratio as a step function of time. Since the main aim of this article was to study the predictive value of type of device, interactions between type of device and the other covariates were systematically tested by comparing models with interactions to models without interactions with likelihood ratio tests. Multivariate Cox models were built using best subset selection, and selected using the Schwarz Bayesian Criterion, Harrell c statistics, and Kent and O'Quigley ρ^2.

Logistic regression analysis was used to identify prognostic factors of acute renal failure (ARF). The log linearity assumption was tested by comparing a model with the continuous covariate with a model including a quadratic component with a F test for nested models, and was visually checked using spline functions plotting the empirical logits against the considered covariate. In case of rejection, the continuous variable was dichotomized so as to maximize the area under the receiver operating characteristic curve (c statistic). Again, interactions between type of device and the other covariates were systematically tested by comparing models with interactions to models without interactions with likelihood ratio tests. Multivariate logistic models were chosen using best subset selection, and selected using Schwarz's Bayesian Criterion, c statistics and *p* of the Hosmer–Lemeshow test.

A two-tailed type I error rate $< .05$ was considered for statistical significance.

RESULTS

Between October 2004 and October 2012, 225 patients met the inclusion criteria. The cut off day for inclusion was November 1, 2012. According to the modified Crawford classification, 21.8% of patients were classified as TAAA types I, II, or III, 10.7% as TAAA types IV or V, and 67.5% as JR-PRAA. The procedure technical failure rate was 2.7%. Four patients died during the first 24 hour post-operative period, including one on-table rupture; four failed vessel catheterizations occurred.

A total of 433 target renal vessels were incorporated in the endovascular repair, including 374 renal fenestrations (FEVAR group) and 53 renal branches (BEVAR group). In 86.9% of patients the bridging stent was a covered stent. The median follow up (CI 95%) was 3.1 (2.9–3.3) years. Both groups were comparable except for aortic aneurysm diameter, previous aortic surgery, and pre-operative CKD. Pre-operative renal measures and pre-operative renal function were also comparable (Table 1).

Mortality

A total of 67 deaths were reported during the study period. The 30 day mortality rate was 6.2% ($n = 14$) and three additional patients suffered aneurysm related mortality during follow up (Table 2). During follow up, 8 patients died from cancer, 10 from cardiac failure, 5 from pulmonary disease, and 15 from other medical diseases. This information was collected prospectively in an electronic database but was not available in 12 patients. There was no evidence of procedure related issues at last follow up in these 12 patients. Multivariate models showed that peripheral artery disease (PAD) (HR = 4.245 [1.752; 10.283], $p = .001$) and left ventricular ejection fraction (LVEF) $< 40\%$ (HR = 5.830 [1.726; 19.693], $p = .005$) were associated with an increased risk of death. In an equivalent multivariate model, ARF before 6 months of follow up and post-operative dialysis before 6 months of follow up were associated with an increased risk of death (HR = 4.497 [1.427; 14.176], $p = .01$) and (OR = 7.853 [2.874; 21.339], $p < .0001$) respectively.

Table 1. Pre-operative demographics, risk factors and renal characteristics.

Pre-operative covariates	Whole sample ($n = 225$)	Fenestrated ($n = 187$)	Multi-branched ($n = 38$)	p
Age at intervention (yrs)	70.5 (8.0)	70.7 (7.7)	69.8 (9.3)	NS
Female	14 (6.2%)	10 (5.4%)	4 (10.5%)	NS
BMI (kg/m^2)	27.6 (4.6)	27.6 (4.6)	27.6 (4.7)	NS
Diameter AA (mm)	60.4 (10.4)	59.4 (9.6)	65.4 (12.6)	.008
Hypertension	178 (79.1%)	148 (79.1%)	30 (79.0%)	NS
Hyperlipidemia	127 (56.4%)	107 (57.2%)	20 (52.6%)	NS
Diabetes mellitus	47 (20.9%)	36 (19.3%)	11 (29.0%)	NS
Smoker				NS
No	35 (15.6%)	28 (15.0%)	7 (18.4%)	
Yes	62 (27.6%)	52 (27.8%)	10 (26.3%)	
Former	128 (56.9%)	107 (57.2%)	21 (55.3%)	
CAD	114 (50.7%)	96 (51.3%)	18 (47.4%)	NS
COPD	95 (42.2%)	83 (44.4%)	12 (31.6%)	NS
CKD	53 (23.6%)	38 (20.3%)	15 (39.5%)	.01
LVEF $< 40\%$	13 (5.8%)	13 (7.0%)	0 (0%)	NS
Arrhythmia	33 (14.7%)	28 (15.0%)	5 (13.2%)	NS
Stroke	28 (12.4%)	22 (11.8%)	6 (15.8%)	NS
PAD	80 (35.6%)	63 (33.7%)	17 (44.7%)	NS
Aortic surgery	55 (24.4%)	36 (19.3%)	19 (50.0%)	$< .0001$
APT	178 (79.1%)	145 (77.5%)	33 (86.8%)	NS
ACE inhibitors	86 (38.2%)	71 (38.0%)	15 (39.5%)	NS
ARBs	67 (29.8%)	52 (27.8%)	15 (39.5%)	NS
Diuretics	56 (24.9%)	48 (25.7%)	8 (21.1%)	NS
Metformin	18 (8.0%)	13 (7.0%)	5 (13.2%)	NS
Statins	163 (72.4%)	135 (72.2%)	28 (73.7%)	NS
VKA	24 (10.7%)	18 (9.6%)	6 (15.8%)	NS
Beta blockers	108 (48.0%)	87 (46.5%)	21 (55.3%)	NS
ASA				NS
2	5 (2.6%)	4 (2.5%)	1 (3.0%)	
3	176 (92.2%)	147 (93.0%)	29 (87.9%)	
4	10 (5.2%)	7 (4.4%)	3 (9.1%)	
Serum creatinine (mg/L)	11.0 (3.9)	10.8 (3.7)	11.9 (4.5)	NS
MDRD (ml/min/1.73 m^2)	77.0 (27.6)	77.7 (26.5)	73.5 (32.8)	NS
Right renal volume (cm^3)	185.8 (46.7)	185.6 (46.0)	190.0 (47.1)	NS
Left renal volume (cm^3)	183.8 (46.6)	182.7 (46.6)	190.0 (47.1)	NS
Total renal volume (cm^3)	365.9 (80.1)	364.1 (78.2)	376.5 (92.0)	NS
Right renal length (mm)	114.6 (14.2)	114.3 (13.4)	116.7 (18.5)	NS
Left renal length (mm)	113.1 (12.6)	113.3 (12.8)	112.1 (11.5)	NS
Mean renal length (mm)	113.7 (11.3)	113.6 (11.1)	114.3 (12.6)	NS
Right renal artery angulation (°)	−30 (−40; −16)	−30 (−40; −17)	−21 (−36; 0)	NS
Left renal artery angulation (°)	−28 (−38; −13)	−29 (−38; −16)	−27 (−41; 45)	NS

ACE = angiotensin converting enzyme; APT = antiplatelet therapy; ARBs = angiotensin II receptor blockers; ASA = American Society of Anesthesiologists; BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstruction pulmonary disease; LFEV = left ventricular ejection fraction; MDRD = modification of diet in renal disease; PAD = peripheral artery disease; VKA = vitamin K antagonists.

Renal function

Post-operative ARF was seen in 64 patients (29%) and hemodialysis was required in 13 (5.9%), and was permanent in one. The new onset of hemodialysis rate was 0.44%. In patients requiring hemodialysis, four early deaths occurred, two as a result of peri-renal hematoma, one in the context of multi-organ failure, and the last one as a consequence of a cardiac failure. Pre-operative CKD was observed in six of 13 patients requiring hemodialysis. Amongst them were the two patients who died following peri-renal hematoma and the patient who required permanent hemodialysis. Post-operative ARF was observed in four of 12 patients who had a dominant or single kidney. It was not associated with any renal adverse events in this subgroup of patients.

At 1 year, 40.7% of patients who experienced post-operative ARF had renal function similar to the baseline level, and the remainder had a decrease in eGFR $> 20\%$ compared with baseline.

During follow up four patients became dialysis dependent. They all had pre-operative CKD and none experienced renal events during follow up. In an adjusted model, CKD was associated with an increased risk of ARF (HR = 5.880 [2.745; 12.595], $p < .0001$). Other independent prognostic covariates were pre-operative metformin treatment (HR = 3.974 [1.303; 12.122], $p = .02$) and procedure time

Table 2. Description of 30 day mortality and aneurysm related mortality during follow up.

Patient	Time of death	Cause of death	Renal complication	Other complication
1	24 hour	Cardiac failure	–	
2	24 hour	Aortic rupture	–	
3	24 hour	Iliac bypass rupture	–	
4	24 hour	Right renal hematoma	ARF	
5	30 day	Multi-organ failure	ARF	Cerebral ischemia Iliac vein bleeding
6	30 day	Multi-organ failure	ARF + HD	Spinal cord ischemia
7	30 day	Multi-organ failure	ARF + HD	Cholesterol emboli
8	30 day	Cardiac failure	ARF + HD	
9	30 day	Cerebral hemorrhage		Endoleak I Bilateral femoral hematoma
10	30 day	Multi-organ failure	ARF	Multiple emboli
11	30 day	Left renal artery rupture	ARF + HD	
12	30 day	Acute myocardial infarction	ARF	
13	30 day	Liver failure	ARF	CT occlusion
14	30 day	Multi-organ failure	ARF + HD	Sepsis
15	Late	Endograft infection		
16	Late	MI (type 3 endoleak and contained rupture)	ARF	
17	Late	SMA occlusion	ARF + HD	Left renal artery thrombosis

ARF = acute renal failure; CT = coeliac trunk; HD = hemodialysis; MI = myocardial infarction; SMA = superior mesenteric artery.

(HR = 1.010 [1.005; 1.015] per minute, $p = .0002$), but not contrast media volume.

Fig. 1A shows the estimated means of eGFR (log transformed) during follow up. In an adjusted multivariate mixed model for log (eGFR) we found an eGFR decrease with time ($p < .0001$), with 1, 2, and 3 year levels significantly lower than pre-operative levels (1, 2, and 3 year mean decrease from pre-operative time estimated at 19.9% [13.1%; 26.2%], $p < .0001$; 21.7% [14.0%; 28.7%], $p < .0001$; 14.3% [3.1%; 24.3%], $p = .02$, respectively).

Renal morphology. In an adjusted multivariate mixed model for log (total renal volume), total renal volume means were significantly different when comparing pre-operative levels to 1 year, 2 year, and 3 year follow up levels (1, 2, and 3 year mean decrease from pre-operative level estimated at 6.8% [3.4%; 10.1%], $p = .0002$; 9.9% [5.5%; 14.0%], $p < .0001$; 14.8% [6.7%; 22.2%], $p = .0006$, respectively). A significant association between total renal volume and eGFR was seen (increase in total volume of 19.4% [12.8%; 26.3%] per log mL/min/1.73 m^2 increase of eGFR, $p < .0001$). Fig. 1B shows the estimated means of total renal volume (log transformed) during follow up. In a multivariate mixed model analyzing the decrease in total volume compared with pre-operative levels (%), adjusted to a decrease in eGFR > 20%, a greater mean decrease in renal volume of about 3.8 [0.4; 7.3] percentage points ($p = .03$) in patients with a decrease in eGFR > 20% was found.

In an adjusted multivariate mixed model for log (mean renal length), means of renal length were significantly different from pre-operative to 1, 2, and 3 year of follow up (1, 2, and 3 year mean decrease from pre-operative level estimated at 3.4% [1.3%; 5.5%], $p = .002$; 5.1% [2.5%; 7.6%], $p = .0002$; 6.3% [0.8%; 11.5%], $p = .02$, respectively), as shown in Fig. 1C. Results also showed a significant association between mean renal length and eGFR (increase in mean renal length of 5.3% [2.1%; 8.7%] per log mL/min/1.73 m^2 increase of eGFR, $p = .001$). In a multivariate mixed model analyzing the decrease in mean renal length compared with pre-operative levels (%), adjusted to renal impairment, no significant decrease in mean renal length in patients with a decrease in GFR > 20% was found.

Renal composite outcome

Intra-operative. Four intra-operative renal events were noted, all in the FEVAR group, but without significant differences between device groups. One left renal artery required an additional self expandable stent to flatten a major kink, without changes in renal function. Another patient was found to have a kinked left renal artery that required an additional balloon expandable stent. Despite this re-intervention, the stent thrombosed 24 hours later and post-operative acute renal failure with an 83% eGFR decrease was observed. This patient died 3 months after the procedure. Two intra-operative endoleaks were observed on digital subtraction angiography: one type III from a left renal artery bridging stent that resolved after re-ballooning, and one endoleak from a failed right renal artery (RRA) catheterization that was covered by a malpositioned fenestrated device. An ilio-right renal bypass was performed during the same procedure. This patient presented with acute renal failure with a 69% decrease in eGFR.

Follow up. The 30 day renal event rate was 1.9% (4 events), all of them in the FEVAR group. During subsequent follow up, 23 renal events were diagnosed, including the four cases in the first 30 days (Table 3). Multivariate analysis did not show a significant influence of CKD on renal composite outcome. The 30 day freedom from renal composite outcome, 95% CI, was 98.6% [95.8; 99.6] and the 5 year freedom from composite outcome was 84.5% [76.5; 89.9], as shown in Fig. 2. During follow up, a renal related endoleak rate of 3.7% was observed.

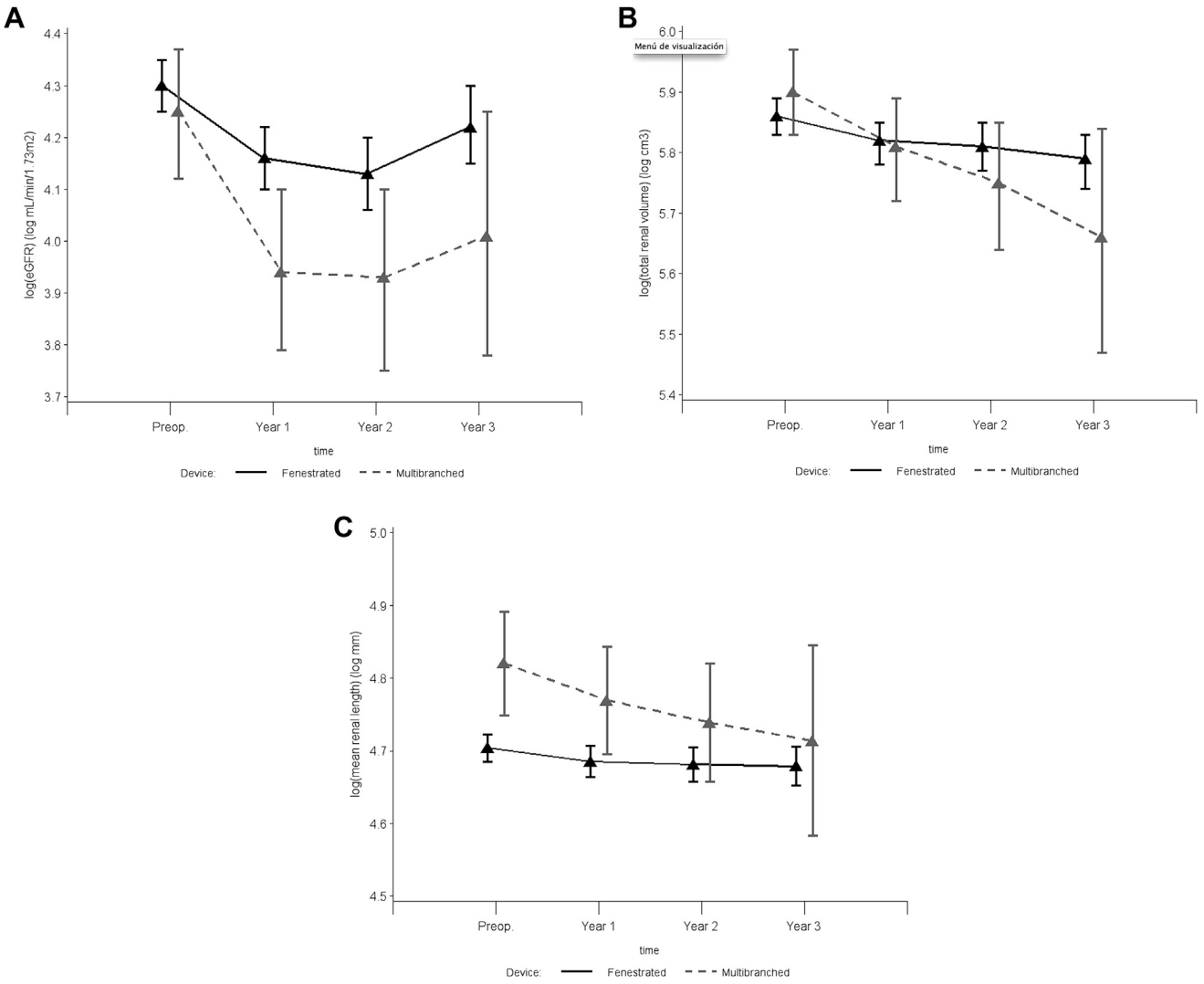


Figure 1. (A) Estimated means of estimated glomerular filtration rate (eGFR) (log-transformed) during follow up. (B) Estimated means of total renal volume (log-transformed) during follow up. (C) Estimated means of mean renal length (log-transformed) during follow up.

The 30 day and follow up renal patency rates were 97.7% and 95.4% respectively. Renal occlusions were observed in 10 patients (4.4%) during follow up. Multivariate analysis showed that the only significant predictor of renal occlusion was accessory renal artery fenestration (HR = 7.960 [1.643; 38.573], $p = .01$). The 30 day freedom from renal occlusion rate was 99.5% [96.7; 99.9] and 5 year freedom from renal occlusion rate 94.4% [89.3; 97.1].

Renal related secondary interventions

During follow up 13 renal related secondary interventions were performed. They included three early procedures (within 30 days of the procedure), all in the FEVAR group. Freedom from renal related secondary intervention is reported in Fig. 3. The 30 day freedom and 5 year freedom from renal related secondary intervention was 98.6 [95.7; 99.5] and 91.2 [84.2; 95.2] respectively.

In a multivariate analysis the only covariate significantly associated with an increased risk was procedure time (HR = 1.011 [1.005; 1.016] per minute, $p = .0003$).

Of note, one patient required device explantation 8 years after the initial procedure because of aneurysm growth with no endoleak identified.

Renal artery angulation

An adjusted multivariate mixed model for each renal artery (RRA and left renal artery [LRA]) angulation showed significantly different outcomes with FEVAR and BEVAR during follow up ($p < .0001$ for both angulations). Following FEVAR, means of renal artery angulation were significantly different when comparing pre-operative to 1, 2, and 3 year follow up (at 3-year mean *increase* from pre-operative measurement estimated at 21.34° [16.45°; 26.22°] for RRA; [15.77°; 26.91°] for LRA ($p < .0001$)). Following BEVAR, opposite results were seen with a 1, 2, and 3 year mean *decrease* compared with pre-operative angle measurements (21.72° [12.51°; 30.93°] ($p < .0001$) for RRA; 10.83° [3.51°; 18.15°] ($p = .004$) for LRA, at 1 year follow up).

Evolution of angulation of RRA and LRA are illustrated in Fig. 4A,B.

Table 3. Renal events during follow up.

Patient	Renal event	Renal artery	DeviceType	Time to event (months)	Pre-op CRD	Pre-op renal stenosis	Secondary intervention	Renal impairment
1	Fracture	Left	Fen	36	No	No		
2	Fracture + occlusion	Left	Fen	2	No	No		↓ 57.3% GFR
3	Type I endoleak	Left	Bran	12	Yes	No		↓ 48.6% GFR
4	Occlusion	A Right Left	Fen Bran	10	No	No		↓ 25.6% GFR
5	Kinking	Right	Bran	24	No	No		
6	Occlusion	Right	Bran	18	No	No		↓ 48.2% GFR
7	Fracture	Right	Bran	42	Yes	No		
8	Dissection	Right	Fen	12	No	No		No
9	Type I endoleak	Left	Bran	36	No	No	Re-stenting	No
10	Stenosis	Left	Fen	2	No	Yes	Re-stenting	↓ 49.4%
11	Type I endoleak Occlusion	Left	Fen	18	Yes	No	Embolization	↓ 80% No
12	Type I endoleak Occlusion	Left	Fen	15	No	No	Embolization	↓ 69% GFR No
13	Stenosis Fracture	Right	Bran	6 21	Yes	Yes	Re-stenting	No
14	Occlusion	Right	Fen	18	Yes	Yes		HD
15	Occlusion	Left	Fen	24 hours	No	No		↓ 81% GFR HD 21 days
16	Stenosis Occlusion Type I endoleak	Left Left Right	Fen Sca	24 81 81	No	No		No ↓ 28% GFR No
17	Endoleak	Left	Fen	4	Yes	No	Re-stenting	No
18	Stenosis	Left	Fen	6 days	No	No	Re-stenting	No
19	Fracture	Left	Fen	39	No	No	Re-stenting	No
20	Type III endoleak	Left	Fen	24	Yes	Yes	Re-stenting	No
21	Type I endoleak	Left	Fen	6 days	No	No	Re-stenting	↓ 67% GFR
22	Fracture	Right	Bran	101	No	No		No
23	Kinking Occlusion	Left	Fen	12 20	No	No		↓ 65.6% GFR

A = accessory; Bran = branch; Fen = fenestration; GFR = glomerular filtration rate; HD = hemodialysis; Sca = scallop.

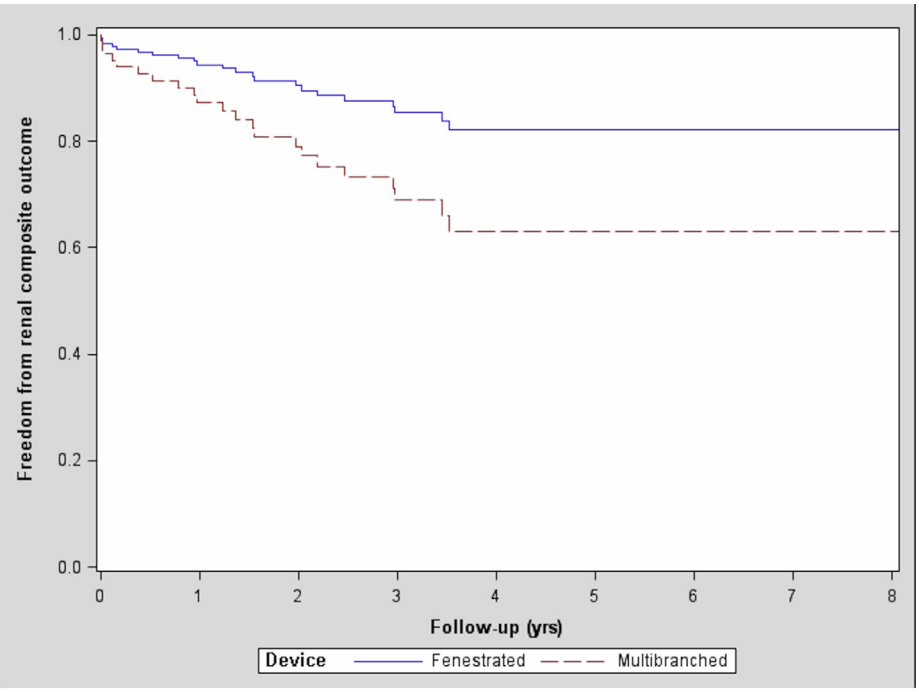
FEVAR vs. BEVAR

Apart from renal artery angulation (detailed above), there were no significant differences in renal outcomes between FEVAR and BEVAR at any endpoint. A significant difference was observed in a univariate analysis, with an increase in renal composite endpoint in the BEVAR group ($p = .02$), associated with an increased relative risk of 2.724 [1.140; 6.510]. All results from the multivariate analyses to determine a device effect are reported in Table 4.

DISCUSSION

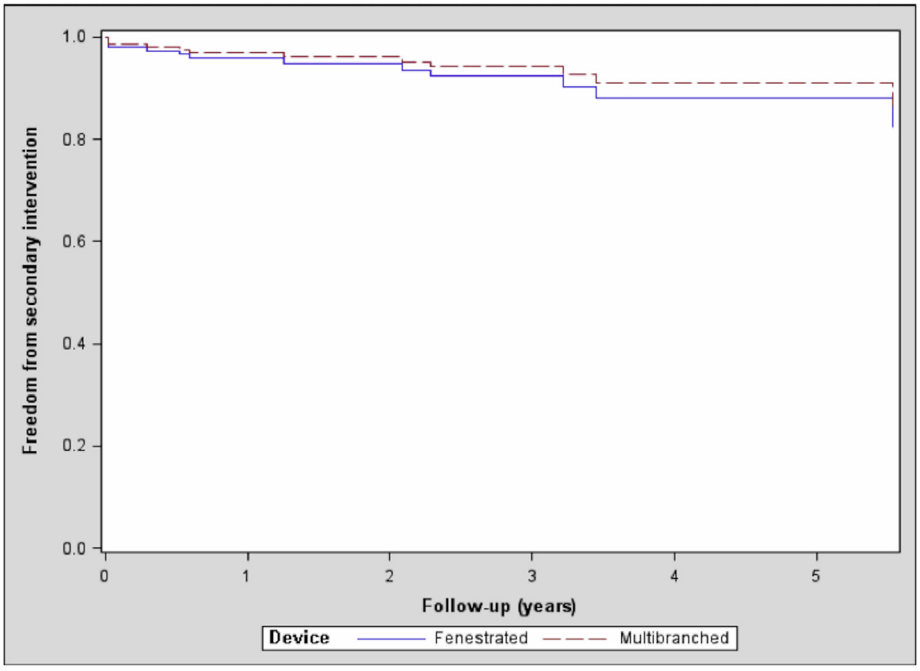
Renal impairment is one of the most frequent major complications after treatment of complex aneurysms. In the current study renal outcomes including renal function (using eGFR MDRD study equation), renal volumes, and renal lengths, and all renal events and their impact on renal function have been analyzed. It was observed that, when the RIFLE criteria were applied to evaluate post-operative renal impairment, 29% of patients experienced a post-operative decrease of eGFR (> 25% compared with baseline), 27.2% in the FEVAR group and 37.8% in BEVAR group (p = ns). Hemodialysis was required in 5.9% of patients, temporarily in all but one case. The new onset of dialysis rate was 0.44%. After 1 year of follow up only 40.7% of patients that had developed post-operative ARF had returned to eGFR baseline levels. Pre-operative CKD, procedure time and pre-operative metformin were identified as risk factors of ARF. ARF, as well as the need for dialysis, were correlated with an increased mortality during the first 6 month post-operative period. No significant differences in renal outcomes and renal secondary interventions were found when comparing FEVAR and BEVAR procedures, as shown by Mastracci et al.[5]

Inconsistent definitions of renal dysfunction make difficult comparisons between different series. Initially, serum creatinine (Scr) was used as a marker of renal dysfunction; however, it is now considered an inaccurate marker because of many factors impacting its level including nutritional intake, medications, age, body mass index (BMI), weight, sex, and race, and its concentration increasing out of normal range only when more than half of the renal function is lost.[14] Subsequently, several validated formulas used for GFR estimation (eGFR), a more accurate measure of renal function, have been developed,[8] but different cut off points to define renal dysfunction have been used. Katsargyris et al.[3] defined renal impairment in their review as a Scr increase > 30%; they reported a renal impairment rate



Year of follow-up	0	1	2	3	4	5	6	7	8
Patients at risk Fen device	186	149	109	73	39	23	8	3	2
Patients at risk Branch device	38	24	19	13	8	4	1	1	1

Figure 2. Freedom from renal composite outcome as estimated by the multivariate Cox model.



Year of follow-up	0	1	2	3	4	5	6	7	8
Patients at risk Fen device	180	153	115	77	41	25	8	3	2
Patients at risk Branch device	33	24	19	13	8	3	0	0	0

Figure 3. Freedom from secondary renal intervention as estimated by the multivariate Cox model.

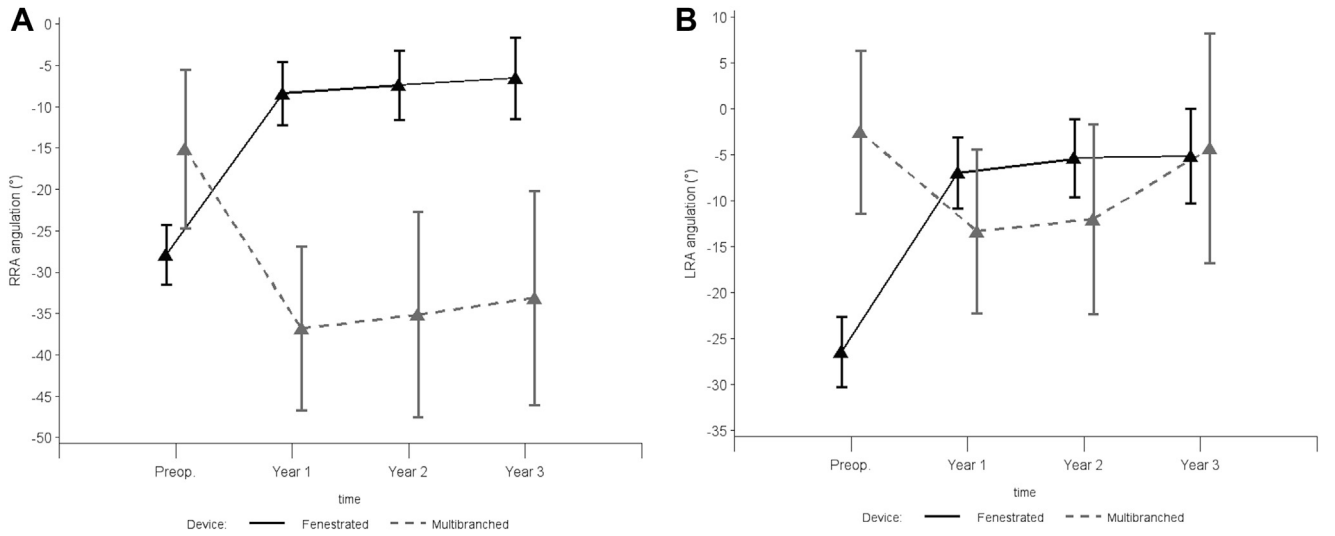


Figure 4. (A) Evolution of right renal angulation during follow up. (B) Evolution of left renal angulation during follow up. LRA = left renal artery; RRA = right renal artery.

after open repair of 18.5% associated with 3.9% of new onset dialysis compared with 9.8% renal dysfunction and 1.5% new dialysis after FEVAR. Recent series evaluating endovascular treatment have shown similar results. Kristmundsson et al.[15] reported a post-operative renal impairment rate of 35%, and Marzelle et al.[16] 18%, with 5.6% of patients requiring dialysis. In these studies early post-procedural renal impairment was associated with technical failure, athero-emboli and contrast nephrotoxicity; a strong correlation between inflammatory and hematological factors and renal impairment has also been described.[17]

Mid- and long-term renal function evolution has been poorly evaluated in the literature after both endovascular and open repairs. Kristmundsson[15] described 22% of patients with a decrease in eGFR of more than 30% during follow up. In comparison, this study shows a significant decrease in renal function during follow up; 36% of patients presented with a decrease in eGFR $>$ 20% after 3 years of follow up. The later subgroup of patients experienced a significant volume decrease that was 3.8% higher than patients with an eGFR decrease $\leq$ 20%. However, mean renal length decrease was similar in both groups and thus seems not to be an accurate or early marker of renal impairment. It seems unlikely that others will adopt measurement of renal volume based on our findings. Although our results may not change follow up protocols, it was interesting to show a continuous diminution in total renal volume during follow up correlated with an eGFR decrease. The clinical relevance of this finding has yet to be ascertained.

Table 4. Comparison of FEVAR and BEVAR in different multivariate analyses for every endpoint.

Endpoint multivariate analysis	BEVAR effect (*p*)
ARF	NS
Postoperative hemodialysis	NS
Decrease eGFR during FU	.01
Decrease total renal volume during FU	NS
Decrease mean length during FU	NS
Renal composite outcome	NS
Renal related endoleak	NS
Renal occlusion	NS
Renal related secondary intervention	NS
Death	NS

ARF = acute renal failure; eGFR = estimated glomerular filtration rate; FU = follow up; NS = not significant.

According to Fillinger's reporting standards,[13] the technical success rate in this study was 95.5%. These results are similar to the published literature with technical success rates ranging from 82.2% to 100%.[11,16,18–21] Analysis of renal events and renal patency and its relation to renal function have been performed to evaluate durability of these devices and to suggest design of branches or fenestrations in relation to aneurysm extent and vessel orientation. Durability of open repair, mid- and long-term renal impairment, and secondary procedures associated with these procedures have been poorly described in the literature. In his review, Katsargyris[3] mentioned only three studies that evaluated renal patency of 88% during follow up. The good results obtained in this study confirm the favorable outcomes associated with endovascular repair. This study reports 30 day and follow up renal patency rates of 97.7% and 95.4% respectively; the 5 year freedom from renal occlusion and freedom from secondary renal intervention rates were 94.4% and 91.2% respectively. These data are similar to the global patency rates of 93.5% described by Verhoeven[22] or 96% described by Kristmundsson.[15] Consequently, it seems probable that target vessel occlusion is more frequently a consequence of technical errors during endograft design or implantation than structural fatigue or neointimal hyperplasia. Delayed renal impairment is largely the result of mechanical device failure. In addition, the type of bridging stent, the choice between fenestrated or branched devices, and the target vessel anatomy have been analyzed in previous studies to

determine their involvement in target vessel patency. Mohabbat et al.[11] have shown a greater rate of occlusion with uncovered stents. Early fenestrated devices were performed with uncovered stents, but since 2006 branched and fenestrated devices have been performed with covered stents. The authors' experience started in 2004, and almost all procedures were performed with covered stents. To assess device durability a rigorous follow up is mandatory. Yearly duplex surveillance is required in addition to CT. Duplex provides a hemodynamic evaluation of bridging stents and target vessels, while CT scans will verify device integrity and positioning.

Renal artery angulation and movements with breathing or anatomy modification after stent implantation have an impact on renal outcomes. In 2005, Draney et al.[23] reported that the right renal artery had greater curvature than the left, as well as a greater change in curvature due to the increased degree of right kidney motion. This increase in curvature and motion may apply more force and stress on stents implanted in this region. A model study from Georgakarakos[24] has analyzed multiple values of take off angle between the renal stent and the endograft. The narrow transitional zone between the bridging stent and the endograft presented the highest stress value correlated with endothelial damage and stent fatigue, and induced local thrombogenic activity compromising lumen patency. This study showed that both renal arteries had increased renal angulation after the procedure, tending to the perpendicular of centerline flow in fenestrated devices. However, with branched devices, left and right artery angulation presented a decrease, trending to the centerline flow. These changes in renal artery angulation have not been identified as risk factors for renal occlusion or for renal composite outcomes, but further study must be undertaken to determine the importance of these changes.

Endoleaks related to renal bridging stents were seen in 3.37% of patients. This may be from material fatigue and stent fracture responsible for type III endoleaks, and from aneurysm disease evolution with component separation responsible for type III endoleaks or with loss of sealing zone responsible for type I endoleaks. Aortic aneurysm is a global disease involving the whole aorta. Device planning is one aspect that is considered integral to long-term durability. It is important not to compromise the landing zone (establishing proximal landing zones in a region of >2 cm parallel walled and thrombus free aorta and of minimal tortuosity) regardless of the number of fenestrations or branches involved. To minimize the risk of component separation, it is also important to plan for at least 75 mm of overlap.

Study limitations

This is a retrospective study that included a limited number of patients. Recent experience was excluded because of a desire to ensure that complete 12 month follow up was observed in all cases. This means that the patients described in this paper were not treated in a hybrid operating room and thus did not undergo completion cone beam CT to assess technical success. This latter examination may reduce the need for early secondary re-interventions.

In a recent study evaluating the natural rate of decline in renal function with age, the authors reported a decline in eGFR of 1.15 mL/min/1.73 m^2 every year in a population >50 years with a baseline clearance above 90 mL/min/1.73 m^2.[25] Another study in a healthy population >65 year olds observed a decline of eGFR of 2.37 mL/min/1.73 m^2 every year.[26] Both studies show that even in healthy populations renal function undergoes a decrease with age; this decrease is probably increased in a vascular patient cohort. It is thus difficult to estimate the influence of mechanical factors in the decline of renal function in the patients enrolled in this study. In addition, without a control group, it is difficult to claim that the reduction in renal volume was related to the intervention.

Reproducibility of angulation measures can also be considered as a limitation. A study performed with the goal of quantifying the amount of variability for inter-observer assessment of aortic neck length and angulation from CTs resulted in highly inconsistent measurements.[27] While slight variations in the measure of renal angulation may exist due to the use of a single reader, inter-observer error was eliminated, as it had been accomplished in the Conway study.[10]

Another limitation of this study was 12 unexplained deaths during follow up. Although patients appeared to have no device related complications at their last known follow up, without an accurate assessment of cause of death it is unclear how to interpret mortality in these 12 patients.

CONCLUSION

FEVAR and BEVAR are durable options for the treatment of complex aortic aneurysms and are associated with low renal morbidity, without differences between these devices. Postoperative ARF increases mortality at 6 months. The clinical impact of decreasing renal volume over time in these patients is yet to be fully understood.

CONFLICT OF INTEREST

Adrien Hertault is a consultant for GE Healthcare. Jonathan Sobocinski is a consultant for Abbott Vascular. Stephan Haulon is a consultant for Cook Medical and GE Healthcare. Tara Mastracii is a consultant for Cook Medical, Maquet and Siemens Imaging.

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REFERENCES

1 Faruqi RM, Chuter TA, Reilly LM, Sawhney R, Wall S, Canto C, et al. Endovascular repair of abdominal aortic aneurysm using a pararenal fenestrated stent-graft. *J Endovasc Surg* 1999;**6**(4):354—8.

2 Chuter TA, Gordon RL, Reilly LM, Goodman JD, Messina LM. An endovascular system for thoracoabdominal aortic aneurysm repair. *J Endovasc Ther* 2001;**8**(1):25—33.

3 Katsargyris A, Oikonomou K, Klonaris C, Töpel I, Verhoeven ELG. Comparison of outcomes with open, fenestrated, and chimney graft repair of juxtarenal aneurysms: are we ready for a paradigm shift? *J Endovasc Ther* 2013;**20**(2):159—69.

4 Nordon IM, Hinchliffe RJ, Holt PJ, Loftus IM, Thompson MM. Modern treatment of juxtarenal abdominal aortic aneurysms with fenestrated endografting and open repair—a systematic review. *Eur J Vasc Endovasc Surg* 2009;**38**(1):35—41.

5 Mastracci TM, Greenberg RK, Eagleton MJ, Hernandez AV. Durability of branches in branched and fenestrated endografts. *J Vasc Surg* 2013;**57**(4):926—33. discussion 933.

6 Reed M, Meier P, Tamhane UU, Welch KB, Moscucci M, Gurm HS. The relative renal safety of iodixanol compared with low-osmolar contrast media: a meta-analysis of randomized controlled trials. *JACC Cardiovasc Interv* 2009;**2**(7):645—54.

7 Heinrich MC, Häberle L, Müller V, Bautz W, Uder M. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology* 2009;**250**(1):68—86.

8 National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;**39**(2 Suppl. 1):S1—266.

9 Bellomo R, Kellum JA, Ronco C. Defining and classifying acute renal failure: from advocacy to consensus and validation of the RIFLE criteria. *Intensive Care Med* 2007;**33**(3):409—13.

10 Conway BD, Greenberg RK, Mastracci TM, Hernandez AV, Coscas R. Renal artery implantation angles in thoracoabdominal aneurysms and their implications in the era of branched endografts. *J Endovasc Ther* 2010;**17**(3):380—7.

11 Mohabbat W, Greenberg RK, Mastracci TM, Cury M, Morales JP, Hernandez AV. Revised duplex criteria and outcomes for renal stents and stent grafts following endovascular repair of juxtarenal and thoracoabdominal aneurysms. *J Vasc Surg* 2009;**49**(4):827—37. discussion 837.

12 Dowdall JF, Greenberg RK, West K, Moon M, Lu Q, Francis C, et al. Separation of components in fenestrated and branched endovascular grafting—branch protection or a potentially new mode of failure? *Eur J Vasc Endovasc Surg* 2008;**36**(1):2—9.

13 Fillinger MF, Greenberg RK, McKinsey JF, Chaikof EL. Society for vascular surgery Ad Hoc Committee on TEVAR reporting standards. Reporting standards for thoracic endovascular aortic repair (TEVAR). *J Vasc Surg* 2010;**52**(4):1022—33. 1033.e15.

14 Sarafidis PA, Bakris GL. Level of kidney function determines cardiovascular fate after coronary bypass graft surgery. *Circulation* 2006;**28;113**(8):1046—7.

15 Kristmundsson T, Sonesson B, Dias N, Törnqvist P, Malina M, Resch T. Outcomes of fenestrated endovascular repair of juxtarenal aortic aneurysm. *J Vasc Surg* 2014;**59**(1):115—20.

16 Marzelle J, Presles E, Becquemin JP, WINDOWS trial participants. Results and factors affecting early outcome of fenestrated and/or branched stent grafts for aortic aneurysms: a multicenter prospective study. *Ann Surg* 2015;**261**:197—206.

17 Chang CK, Chuter TAM, Niemann CU, Shlipak MG, Cohen MJ, Reilly LM, et al. Systemic inflammation, coagulopathy, and acute renal insufficiency following endovascular thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2009;**49**(5):1140—6.

18 Haddad F, Greenberg RK, Walker E, Nally J, O'Neill S, Kolin G, et al. Fenestrated endovascular grafting: the renal side of the story. *J Vasc Surg* 2005;**41**(2):181—90.

19 Bicknell CD, Cheshire NJW, Riga CV, Bourke P, Wolfe JHN, Gibbs RGJ, et al. Treatment of complex aneurysmal disease with fenestrated and branched stent grafts. *Eur J Vasc Endovasc Surg* 2009;**37**(2):175—81.

20 Semmens JB, Lawrence-Brown MMD, Hartley DE, Allen YB, Green R, Nadkarni S. Outcomes of fenestrated endografts in the treatment of abdominal aortic aneurysm in Western Australia (1997—2004). *J Endovasc Ther* 2006;**13**(3):320—9.

21 Reilly LM, Rapp JH, Grenon SM, Hiramoto JS, Sobel J, Chuter TAM. Efficacy and durability of endovascular thoracoabdominal aortic aneurysm repair using the caudally directed cuff technique. *J Vasc Surg* 2012;**56**(1):53—63. discussion 63—4.

22 Verhoeven ELG, Vourliotakis G, Bos WTGJ, Tielliu IFJ, Zeebregts CJ, Prins TR, et al. Fenestrated stent grafting for short-necked and juxtarenal abdominal aortic aneurysm: akn 8-year single centre experience. *Eur J Vasc Endovasc Surg* 2010;**39**(5):529—36.

23 Draney MT, Zarins CK, Taylor CA. Three dimensional analysis of renal artery bending motion during respiration. *J Endovasc Ther* 2005;**12**(3):380—6.

24 Georgakarakos E, Xenakis A, Georgiadis GS, Argyriou C, Antoniou GA, Schoretsanitis N, et al. The hemodynamic impact of misalignment of fenestrated endografts: a computational study. *Eur J Vasc Endovasc Surg* 2014;**47**(2):151—9.

25 Cohen E, Nardi Y, Krause I, Goldberg E, Milo G, Garty M, et al. A longitudinal assessment of the natural rate of decline in renal function with age. *J Nephrol* 2014;**19** [Epub ahead of print].

26 Rifkin DE, Shlipak MG, Katz R, Fried LF, Siscovick D, Chonchol M, et al. Rapid kidney function decline and mortality risk in older adults. *Arch Intern Med* 2008;**168**(20):2212—8.

27 Diehm N, Katzen BT, Samuels S, Pena C, Powell A, Dick F. Sixty-four-detector CT angiography of infrarenal aortic neck length and angulation: prospective analysis of interobserver variability. *J Vasc Interv Radiol* 2008;**19**(9):1283—8.